UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,362	03/22/2004	Thierry Glauser	50623.351	3954

7590 05/10/2010

Cameron Kerrigan
Squire, Sanders & Dempsey L.L.P.
Suite 300
One Maritime Plaza
San Francisco, CA 94111

EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
05/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/807,362	GLAUSER ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2009 and 19 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55,62,66-99 and 103-115* is/are pending in the application.

4a) Of the above claim(s) *1-42 and 66-99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-55,62 and 103-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/09, 4/1/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Note to Applicant: References to paragraphs in non-patent literature refer to full paragraphs (e.g. 'page 1 column 1 paragraph 1' refers to the first full paragraph on page 1 in column 1 of the reference)

Election/Restrictions

To summarize the current election, applicants elected group III, without traverse.

Claims 1-42 and 66-99 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions.

MAINTAINED REJECTIONS

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 43 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 12, and 20 of copending Application No. 11/171111. The claims of the copending application and that of the instant application both teach a medical device with a coating where the coating is composed of polymers that contain in their chain a backbone, along with combinations of moieties that include phosphoryl choline, poly(vinyl pyrrolidone) and hyaluronic acid. They also teach the presence of a bioactive in the coating. Therefore claim 43 is obvious over claims 1, 12, and 20 of copending Application No. 11/171111.

This is a provisional obviousness-type double patenting rejection.

NEW REJECTIONS

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 103-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 103 recites glycerine and 2-hydroxyl-1,3-propylene diamine while claim 104 recites hydroxyl-ε-caprolactone and β-hydroxylmethylbutyrolactone. These recitations do not appear in the disclosure as filed and therefore constitute new matter. Claims 105-115 depend from claims containing new matter therefore they also lack adequate written description as required. In addition claims 103, 109, and 112 recite polymers that have components derived from substituted ε-caprolactone, substituted β-butyrolactone, glycerine or 2-hydroxyl-1, 3-propylene diamine along with a non-degradable backbone. It is not clear that such an embodiment was contemplated at the time of the invention, particularly in the instance of the specific non-degradable polymers recited in claims 109 and 112. This again is new matter.

The specification discloses chemicals, such as ε-caprolactone which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim 103 is directed to encompass "components derived from substituted ε-caprolactone, substituted β-butyrolactone, glycerine or 2-hydroxyl-1, 3-propylene diamine," which only correspond in some undefined way to specifically instantly disclosed chemicals. The full breadth of these derivatives do not meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written

description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives. While some components derived from substituted ε-caprolactone, substituted β-butyrolactone, glycerine or 2-hydroxyl-1,3-propylene diamine are described by the prior art, since applicant provides no guidance regarding the chemical modifications necessary to produce their envisioned components derived from substituted ε-caprolactone, substituted β-butyrolactone, glycerine or 2-hydroxyl-1,3-propylene diamine, one of ordinary skill in the art cannot predictably generate and utilize any possible components derived from substituted ε-caprolactone, substituted β-butyrolactone, glycerine or 2-hydroxyl-1,3-propylene diamine in accordance with the invention as claimed. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997);

In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, the full breadth of the claim does not meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.) Claims 104-115 depend from claim 103 and do not remedy its lack of adequate written description; therefore these claims also are not sufficiently described.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 112 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 112, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 43-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilborn et al.(previously cited) in view of Koulik et al.(previously cited), Marchant (previously cited), and Wright et al.(previously cited).

Hilborn et al. teach a medical device with a copolymer coating that includes a phospholipid within the biodegradable polymer chain (see abstract and page 7 lines 19-28). Stents are named as particular medical devices that are envisioned (see claims 15-16). Hilborn et al. also teach that the coatings are loaded with a biologically active agent (see claims 13-14). These coatings are taught for conferring biocompatibility and reduced protein adhesion to the device surface (see page 3 lines 14-28). Specifically a copolymer of poly(ε-caprolactone) with phosphatidyl choline is taught (see page 11 lines 4-12; instant claims 43 and 47-48). In addition to phosphatidyl choline, phosphatidyl serine and zwitterionic phosphatidyl ethanolamine are also taught as being equally suitable as phospholipids in the taught polymers (see page 8 lines 1-7; instant claim 43). It is known that phosphoryl choline is contained within the structure of phosphatidyl choline, as is phosphoryl serine within phosphatidyl serine and phosphoryl ethanolamine within phosphatidyl ethanolamine. Therefore, a poly(ε-caprolactone)-phosphatidyl choline polymer comprises both a biodegradable polymer and the claimed phospholipid phosphoryl choline (see instant claim 43). Hilborn et al. also teach that

similar polymers have been made using non-biodegradable polymers that include polymethacrylates, polysulfones, polyethylenes and polystyrenes (see page 3 lines 14-20; instant claim 49). Hilborn et al. do not specifically teach rapamycin as a biologically active agent in the coating or heparin bound to the polymer via an anti-fouling moiety.

Koulik et al. teach a medical device with a biocompatible coating where a phosphoryl choline macromer, polybutylmethacrylate (acrylic polymer) and heparin are included in the same polymer (see abstract; instant claim 46). The presence of the heparin, in addition to the phosphoryl choline is taught to reduce thrombogenicity (see paragraph 25).

Marchant teaches medical devices with polymer coatings that are resistant to protein deposition and coagulation (thrombogenesis) (see column 3 lines 2-5). Similar to Koulik et al., Marchant also teaches heparin as an anti-thrombogenic agent attached to the polymer (see column 3 lines14-15; instant claims 54 and 60). Marchant also teaches that the heparin is attached to the polymer via a spacer arm such that the surface can be non-thrombogenic without adversely affecting the bulk properties of the polymer coating (see column 3 lines 11-13 and 19-21). Additionally, the spacer is taught to be poly (ethylene oxide) (PEG) which provides a solvated surface for the device and lifts the heparin off the surface of the device (see column 3 line 65-column 4 line 7; instant claims 43 and 50-55).

Wright et al. teach a polymer coating on a medical device where bioactive agents are chemically linked to the polymer coating. In particular, Wright et al. teach that rapamycin is bound to or mixed with the polymer coating of a medical device to confer

anti-restenotic properties to the device surface (see column 1 lines 8-13; instant claims 44-45).

Since both Hilborn et al. and Koulik et al. teach phospholipid containing polymers as biocompatible coatings on medical devices, it would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Koulik et al. in the invention of Hilborn et al. to add heparin to their taught polymer and further improve the biocompatibility of their taught coated stent (e.g. less thrombogenic). In addition, Koulik et al. teach polybutylmethacrylate in their phosphoryl choline containing polymer which is within the set of polymethacrylates envisioned in the polymer of Hilborn et al. So it also would have been obvious to utilize polybutylmethacrylate as a particular non-degradable polymer in the invention of Hilborn et al. Given the teachings of Marchant that teach the benefit of binding heparin to a polymer coating via a PEG spacer, this ordinarily skilled artisan would have been motivated to use this attachment scheme in the device of Hilborn et al. in view of Koulik et al. Further, based upon Wright et al. who teach the inclusion of rapamycin in stent coatings to act against restenosis, it would have been obvious to also include this anti-restenotic compound in the stent coating of Hilborn et al. in view of Koulik et al. and Marchant. Therefore claims 43-55 are obvious over Hilborn et al. in view of Koulik et al., Marchant and Wright et al.

Claims 43, 45, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilborn et al. in view of Koulik et al., Marchant and Wright et al. as

applied to claims 43-55 above, and further in view of Uhrich et al. (previously cited) and Falatico et al. (previously cited).

Hilborn et al. in view of Koulik et al., Marchant and Wright et al. make obvious a stent that includes a coating composed of a polyester polymer that contains rapamycin and includes phosphoryl choline moieties as well as heparin bound via PEG spacers bound to the polymer. This modified reference does not specifically teach a polymer backbone that degrades into pharmacologically active components that act in the process of restenosis or sub-acute-thrombosis.

Uhrich et al. teach a polyanhydride ester polymer that degrades into the anti-inflammatory salicylic acid (therapeutically active in sub-acute thrombosis, interpreted as equivalent to PolyAspirin™) (see example 1; instant claim 62). These polymers are taught used in implanted medical devices (see paragraph 12). In addition, Uhrich et al. also teach that other biologically active molecules can be included with these polymers and in particular, are covalently bound to these polymers (see paragraph 15).

Falatico et al. teach stents that are coated with a polymer coating that contains multiple drugs (see paragraphs 31 and 33). In particular, Falatico et al. teach the combination of anti-inflammatory agents with rapamycin and heparin in such a surface coating (see paragraph 62)

In light of the teachings of Uhrich et al. and Falatico et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to use their salicylic acid producing polyanhydride ester polymer as the biodegradable polyester in the polymer taught by Hilborn et al. in view of Koulik et al., Marchant and Wright et al.

This would yield a coating that included rapamycin with a polymer that comprises phosphoryl choline, heparin bound via a PEG spacer and a backbone that degrades into pharmacologically active components that act in the process of restenosis or sub-acute-thrombosis. This combination is supported by the teachings of Falatico et al. that point to the benefit of combining an anti-inflammatory agent with rapamycin and heparin in a stent coating. Therefore claims 43, 45, and 62 are obvious over Hilborn et al. in view of Koulik et al., Marchant, Wright et al., Uhrich et al. and Falatico et al.

Claims 43-45, 47-48, and 103-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toner et al. (US PGPub No. 2004/0180039 – see IDS) in view of Durrani et al. (Biomaterials 1986 7:121-125) and Gautier et al. (Journal of Biomaterial Science Polymer Edition 2003 14:63-85).

Toner et al. teach implantable medical devices that include a polymeric layer loaded with a beneficial agent (see claim 1). This polymeric layer is taught to have phosphoryl choline as a pendant group (see claim 22; instant claims 43, 103, and 105). Toner et al. teach poly(ε-caprolactone), silicones, poly(vinylpyrrolidone) and copolymers thereof as envisioned polymers in this layer (see paragraph 71). Thus copolymers of poly(ε-caprolactone) with silicones or poly(vinylpyrrolidone) are envisioned (see instant claims 43, 47-48, and 109-114). Rapamycin is taught as an envisioned beneficial agent and stents are envisioned devices (see paragraph 59 and claim 24; instant claims 44-45 and 107-108). Toner et al. do not explicitly teach how the phosphoryl choline is attached to the poly(ε-caprolactone) polymer.

Durrani et al. teach the attachment of phosphoryl choline moieties to polymer surfaces to improve their thromboresistance (see page 121 column 1-column 2 paragraph 1). Specifically, Durrani et al. teach reactive phosphoryl choline compounds that react with hydroxyl groups on polymer surfaces to achieve this modification(see page 124 column 1 paragraph 2; instant claim 106).

Gautier et al. teach that the modification of poly(ε-caprolactone) has been difficult due to its lack of reactive functional groups but suggest a means of introducing such functionality into this polymer (see page 64 paragraph 1 and page 65 paragraph 1). Specifically, Gautier et al. prepare poly(ε-caprolactone) with pendant hydroxyl groups (interpreted as "derived from hydroxyl-ε-caprolactone) (see Scheme 1a; instant claims 103-104).

It would have been obvious to one of ordinary skill in the art to prepare the device of Toner et al. with the rapamycin containing coating composed of poly(ε-caprolactone) or a poly(ε-caprolactone) copolymer (e.g. with a silicone or poly(vinylpyrrolidone)) having pendant phosphoryl choline moieties attached via hydroxyl groups on the caprolactone chain/moieties as taught by Gautier et al. Since Durrani et al. teach the benefit of phosphoryl choline on polymer surfaces attached via hydroxyl groups and Gautier et al. teach how to incorporate pendant hydroxyl groups into caprolactone polymers, this ordinarily skilled artisan would have been motivated to make this modification to Toner et al. and had a reasonable expectation of success. Therefore claims 43-45, 47-48, and 103-114 are obvious over Toner et al. in view of Durrani et al. and Gautier et al.

Claims 43, 45-46, 49-55, 103, and 113-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toner et al. in view of Durrani et al. and Gautier et al. as applied to claims 43-45, 47-48, and 103-112 above, and further in view of Marchant.

Toner et al. in view of Durrani et al. and Gautier et al. make obvious an implantable device with a rapamycin containing coating composed of poly(ε-caprolactone) or a poly(ε-caprolactone) copolymer (e.g. with a silicone or poly(vinylpyrrolidone)) having pendant phosphoryl choline moieties attached via hydroxyl groups on the caprolactone chain/moieties. This modified reference does not explicitly teach heparin bound to the polymer.

Marchant teaches medical devices with polymer coatings that are resistant to protein deposition and coagulation (thrombogenesis) (see column 3 lines 2-5). Marchant teaches heparin as an anti-thrombogenic agent attached to the polymer to facilitate this resistance (see column 3 lines14-15; instant claims 54 and 60). Marchant also teaches that the heparin is attached to the polymer via a spacer arm such that the surface can be non-thrombogenic without adversely affecting the bulk properties of the polymer coating (see column 3 lines 11-13 and 19-21). Additionally, the spacer is taught to be poly (ethylene oxide) (PEG) which provides a solvated surface for the device and lifts the heparin off the surface of the device (see column 3 line 65-column 4 line 7; instant claims 43 and 50-55).

Given the teachings of Marchant that cite the benefits of binding heparin to a polymer coating via a PEG spacer, one of ordinary skill in the art at the time of the

invention would have found it obvious to use this attachment scheme in the coating of Toner et al. in view of Durrani et al. and Gautier et al. In the instance where the coating included a poly(ε-caprolactone) copolymer (e.g. with a silicone or poly(vinylpyrrolidone), the polymer comprise a non-degradable polymer in its backbone, phospholipid moieties, non-fouling moiety, caprolactone, and heparin bound via a PEG spacer (see instant claims 46, 49-55, and115). Therefore claims 43, 45-46, 49-55, 103, and 113-115 are obvious over Toner et al. in view of Durrani et al., Gautier et al., and Marchant.

Claims 43, 45, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toner et al. in view of Durrani et al., Gautier et al., Uhrich et al. Falatico et al., and Marchant.

Toner et al. teach implantable medical devices that include a polymeric layer loaded with a beneficial agent (see claim 1). This polymeric layer is taught to have phosphoryl choline as a pendant group (see claim 22; instant claim 43). Toner et al. teach poly(ε-caprolactone) and polyanhydrides as well as copolymers thereof as envisioned polymers in this layer (see paragraph 71). Toner et al. do not explicitly teach how the phosphoryl choline is attached to the poly(ε-caprolactone) polymer or heparin attached to the polymer.

Durrani et al. teach the attachment of phosphoryl choline moieties to polymer surfaces to improve their thromboresistance (see page 121 column 1-column 2 paragraph 1). Specifically, Durrani et al. teach reactive phosphoryl choline compounds

that react with hydroxyl groups on polymer surfaces to achieve this modification (see page 124 column 1 paragraph 2).

Gautier et al. teach that the modification poly(ε-caprolactone) has been difficult due to its lack of reactive functional groups but suggest a means introducing such functionality into this polymer (see page 64 paragraph 1 and page 65 paragraph 1). Specifically, Gautier et al. prepare poly(ε-caprolactone) with pendant hydroxyl groups (interpreted as "derived from hydroxyl-ε-caprolactone) (see Scheme 1a).

Falatico et al. teach stents that are coated with a polymer coating that contains multiple drugs (see paragraphs 31 and 33). In particular, Falatico et al. teach the combination of anti-inflammatory agents with rapamycin and heparin in such a surface coating (see paragraph 62; instant claim 45)

Uhrich et al. teach a polyanhydride ester polymer that degrades into the anti-inflammatory salicylic acid (therapeutically active in sub-acute thrombosis, interpreted as equivalent to PolyAspirin™) (see example 1; instant claim 62). These polymers are taught used in implanted medical devices (see paragraph 12). In addition, Uhrich et al. also teach that other biologically active molecules can be included with these polymers and in particular, are covalently bound to these polymers (see paragraph 15).

Marchant teaches medical devices with polymer coatings that are resistant to protein deposition and coagulation (thrombogenesis) (see column 3 lines 2-5). Marchant teaches heparin as an anti-thrombogenic agent attached to the polymer to facilitate this resistance (see column 3 lines14-15). Marchant also teaches that the heparin is attached to the polymer via a spacer arm such that the surface can be non-

thrombogenic without adversely affecting the bulk properties of the polymer coating (see column 3 lines 11-13 and 19-21). Additionally, the spacer is taught to be poly (ethylene oxide) (PEG) which provides a solvated surface for the device and lifts the heparin off the surface of the device (see column 3 line 65-column 4 line 7; instant claim 43).

In light of the teachings of Uhrich et al. and Falatico et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to use their salicylic acid producing polyanhydride ester polymer as the polyanhydride taught by Toner et al. Since Durrani et al. teach the benefit of phosphoryl choline on polymer surfaces attached via hydroxyl groups and Gautier et al. teach how to incorporate pendant hydroxyl groups into caprolactone polymers, this ordinarily skilled artisan would have been motivated to make this modification to the poly(ε-caprolactone) and polyanhydride ester copolymer Toner et al. in view of Uhrich et al. and Falatico et al. Moreover attachment of heparin to this polymer via a PEG spacer as taught by Marchant would have further facilitated the anti-thrombogenicity of the layer. Therefore claims 43, 45, and 62 are obvious over Toner et al. in view of Durrani et al., Gautier et al., Uhrich et al. Falatico et al., and Marchant.

Response to Arguments

Applicants' arguments, filed February 5, 2009 and May 19, 2009, have been fully considered but they are not deemed to be persuasive or moot in light of the new grounds of rejection.

Only the arguments regarding the rejection over Hilborn et al. in view of Koulik et al., Marchant and Wright et al. is pertinent to both the instant claims and not made moot in light of the new grounds of rejection. Applicants argue that this combination of references does not teach the instant claims because Hilborn et al. in view of Koulik et al. and Wright et al. do not teach a non-fouling moiety as recited in the claims and Marchant also does not teach such a moiety. Merchant explicitly teaches poly(ethylene oxide), which is the same as PEG, as a spacer molecule that joins an anticoagulant to a polymer layer on a device (see column 3 line 654-column 4 line 7). Heparin is taught as the anticoagulant (see column 3 lines 14-15). Applicant names PEG as an anti-fouling moiety; therefore the combination of Hilborn et al. in view of Koulik et al., Marchant and Wright et al. as discussed above does in fact teach a non-fouling moiety as claimed.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/S. TRAN/
Primary Examiner, Art Unit 1615